

What is claimed is:

1. A computer implemented method for calculating a normalization factor comprising:

providing a first intensity value ( $I^{(1)}$ ) of a probe in a first probe array and a

5 second intensity value ( $I^{(2)}$ ) of said probe in a second probe array;

obtaining the geometric mean ( $x$ ) of said  $I^{(1)}$  and said  $I^{(2)}$ ;

calculating said normalization factor according to:

$f(x) = e^{h(x)}$ , wherein said  $h(x)$  is derived from referential intensities from

said first and second probe arrays.

2. The method of Claim 1 wherein said  $h(x)$  is derived by relating geometric means ( $x_i$ ) of first referential intensities ( $RI_i^{(1)}$ ) in the first probe array and second referential intensities ( $RI_i^{(2)}$ ) in the second probe array to:

$$y_i = \log \left( \frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

3. The method of Claim 2 wherein said relating comprising:

sorting ( $x_i, y_i$ ) pairs according to  $x_i$  into a plurality ( $m$  number) of bins with no overlapping;

computing medians ( $\bar{x}_k$ ) of  $x_i$ 's and medians ( $\bar{y}_k$ ) of  $y_i$ 's for each bin; and

20 interpolating said medians ( $\bar{x}_k, \bar{y}_k$ ).

4. The method of Claim 3 wherein said bins are of approximately equal size.

5. The method of Claim 4 wherein said  $h(x)$  is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_1 + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_{i+1}), w = \frac{\bar{x}_{i+1} + 1 - x}{\bar{x}_{i+1} + 1 - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

6. The method of Claim 5 wherein said  $m$  is 3.

7. A computer implemented method for comparing the expression of a gene in a first sample with a second sample comprising:

providing a first plurality of intensity values ( $I_i^{(1)}$ ), each of which reflects the expression of said gene in said first sample, wherein said intensity values are obtained from a first nucleic acid probe array;

providing a second plurality of intensity values ( $I_i^{(2)}$ ), each of which reflects the expression of said gene in said second sample, wherein said intensity values are obtained from a second nucleic acid probe array;

calculating a  $p$ -value using one-sided Wilcoxon's signed rank test, wherein the  $p$ -value is for a null hypothesis that  $median(f(x)I_i^{(2)} - I_i^{(1)}) = 0$  and an alternative

hypothesis that  $\text{median}((f(x)I_i^{(1)} - I_i^{(2)}) > 0$ , wherein said  $f(x)$  is a normalization factor; and

indicating whether said transcript is present based upon said  $p$ -value.

- 5      8.      The method of Claim 7 further comprising a step of calculating normalization factor, said step comprising:

obtaining the geometric mean ( $x$ ) of said  $I_i^{(1)}$  and said  $I_i^{(2)}$  ;

calculating said normalization factor according to:

$f(x) = e^{h(x)}$ , wherein said  $h(x)$  is derived from referential intensities from

10      said first and second probe arrays.

9.      The method of Claim 8 wherein said  $h(x)$  is derived by relating geometric means ( $x_i'$ ) of first referential intensities ( $RI_i^{(1)}$ ) in said first probe array and said second referential intensities ( $RI_i^{(2)}$ ) in said second probe array to:

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$$y_i' = \log \left( \frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

10.      The method of Claim 9 wherein said relating comprising:

sorting ( $x_i, y_i$ ) pairs according to  $x_i$  into a plurality ( $m$  number) of bins with no overlapping;

20      computing medians ( $\bar{x}_k$ ) of  $x_i$ 's and medians ( $\bar{y}_k$ ) of  $y_i$ 's for each bin; and

interpolating said medians  $(\bar{x}_k, \bar{y}_k)$ .

11. The method of Claim 10 wherein said bins are of approximately equal size.

5 12. The method of Claim 11 wherein said  $h(x)$  is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_i + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_i + 1], w = \frac{\bar{x}_{i+1} - x}{\bar{x}_{i+1} - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

13. The method of Claim 12 wherein said  $m$  is 3.

14. A system for calculating a normalization factor comprising:

10 a processor; and

a memory coupled with the processor, the memory storing a plurality of machine instructions that cause the processor to perform a plurality of logical steps when implemented by the processor, the logical steps comprising:

providing a first intensity value  $I^{(1)}$  of a probe in a first probe array and a

15 second intensity value  $I^{(2)}$  of said probe in a second probe array;

obtaining the geometric mean  $(x)$  of said  $I^{(1)}$  and said  $I^{(2)}$ ;

calculating said normalization factor according to:

$f(x) = e^{h(x)}$ , wherein said  $h(x)$  is derived from referential intensities from

said first and second probe arrays.

15. The system of Claim 14 wherein said  $h(x)$  is derived by relating geometric means  $(x_i')$  of first referential intensities  $(RI_i^{(1)})$  in the first probe array and second referential intensities  $(RI_i^{(2)})$  in the second probe array to:

$$y_i = \log \left( \frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

16. The system of Claim 15 wherein said relating comprising:  
 sorting  $(x_i, y_i)$  pairs according to  $x_i$  into a plurality ( $m$  number) of bins with no overlapping;

- 10 computing medians  $(\bar{x}_k)$  of  $x_i$ 's and medians  $(\bar{y}_k)$  of  $y_i$ 's for each bin; and  
 interpolating said medians  $(\bar{x}_k, \bar{y}_k)$ .

17. The system of Claim 16 wherein said bins are of approximately equal size.

- 15 18. The system of Claim 17 wherein said  $h(x)$  is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_1 + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_{i+1}), w = \frac{\bar{x}_{i+1} + 1 - x}{\bar{x}_{i+1} + 1 - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

19. The system of Claim 18 wherein said  $m$  is 3.

20. A system for comparing the expression of a gene in a first sample with a second sample comprising:

a processor; and

a memory coupled with the processor, the memory storing a plurality of machine instructions that cause the processor to perform a plurality of logical steps when implemented by the processor, the logical steps comprising:

providing a first plurality of intensity values ( $I_i^{(1)}$ ), each of which reflects the expression of said gene in said first sample, wherein said intensity values are obtained from a first nucleic acid probe array;

providing a second plurality of intensity values ( $I_i^{(2)}$ ), each of which reflects the expression of said gene in said second sample, wherein said intensity values are obtained from a second nucleic acid probe array;

calculating a  $p$ -value using one-sided Wilcoxon's signed rank test, wherein the  $p$ -value is for a null hypothesis that  $median(f(x) I_i^{(2)} - I_i^{(1)}) = 0$  and an alternative hypothesis that  $median((f(x) I_i^{(1)} - I_i^{(2)})) > 0$ , wherein said  $f(x)$  is a normalization factor; and

indicating whether said transcript is present based upon said  $p$ -value.

21. The system of Claim 20 further comprising a step of calculating normalization factor, said step comprising:

obtaining the geometric mean ( $x$ ) of said  $I_i^{(1)}$  and said  $I_i^{(2)}$ ;

calculating said normalization factor according to:

$f(x) = e^{h(x)}$ , wherein said  $h(x)$  is derived from referential intensities from

said first and second probe arrays.

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22. The system of Claim 21 wherein said  $h(x)$  is derived by relating geometric means ( $x_i'$ ) of first referential intensities ( $RI_i^{(1)}$ ) in said first probe array and said second referential intensities ( $RI_i^{(2)}$ ) in said second probe array to:

$$y_i' = \log \left( \frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

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23. The system of Claim 22 wherein said relating comprising:  
 sorting ( $x_i, y_i$ ) pairs according to  $x_i$  into a plurality ( $m$  number) of bins with no overlapping;

computing medians ( $\bar{x}_k$ ) of  $x_i$ 's and medians ( $\bar{y}_k$ ) of  $y_i$ 's for each bin; and

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interpolating said medians ( $\bar{x}_k, \bar{y}_k$ ).

24. The system of Claim 23 wherein said bins are of approximately equal size.

25. The system of Claim 24 wherein said  $h(x)$  is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_i + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_i + 1], w = \frac{\bar{x}_{i+1} - x}{\bar{x}_{i+1} - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

26. The system of Claim 25 wherein said  $m$  is 3.

27. A computer software product for calculating a normalization factor comprising:  
 computer program code for providing a first intensity value ( $I^{(1)}$ ) of a probe  
 in a first probe array and a second intensity value ( $I^{(2)}$ ) of said probe in a second  
 probe array;

computer program code for obtaining the geometric mean ( $x$ ) of said  $I^{(1)}$   
 and said  $I^{(2)}$ ;

computer program code for calculating said normalization factor according  
 to:

$$f(x) = e^{h(x)}, \text{ wherein said } h(x) \text{ is derived from referential intensities from}$$

said first and second probe arrays; and

a computer readable medium for storing said codes.

28. The computer software product of Claim 27 wherein said  $h(x)$  is derived by  
 relating geometric means ( $x_i$ ) of first referential intensities ( $RI_i^{(1)}$ ) in the first  
 probe array and second referential intensities ( $RI_i^{(2)}$ ) in the second probe array to:



$$y_i = \log \left( \frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

29. The computer software product of Claim 28 wherein said code for relating comprising:

computer program code for sorting  $(x_i, y_i)$  pairs according to  $x_i$  into a plurality ( $m$  number) of bins with no overlapping;

computer program code for computing medians  $(\bar{x}_k)$  of  $x_i$ 's and medians  $(\bar{y}_k)$  of  $y_i$ 's for each bin; and

computer program code for interpolating said medians  $(\bar{x}_k, \bar{y}_k)$ .

30. The computer software product of Claim 29 wherein said bins are of approximately equal size.

31. The computer software product of Claim 30 wherein said  $h(x)$  is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_1 + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_{i+1}), w = \frac{\bar{x}_{i+1} + 1 - x}{\bar{x}_{i+1} + 1 - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

32. The computer software product of Claim 31 wherein said  $m$  is 3.

33. A computer software product for comparing the expression of a gene in a first sample with a second sample comprising:

computer program code for providing a first plurality of intensity values ( $I_i^{(1)}$ ), each of which reflects the expression of said gene in said first sample,

5 wherein said intensity values are obtained from a first nucleic acid probe array;

computer program code for providing a second plurality of intensity values ( $I_i^{(2)}$ ), each of which reflects the expression of said gene in said second sample,

wherein said intensity values are obtained from a second nucleic acid probe array;

computer program code for calculating a  $p$ -value using one-sided Wilcoxon's signed rank test, wherein the  $p$ -value is for a null hypothesis that  $median(f(x) I_i^{(2)} - I_i^{(1)}) = 0$  and an alternative hypothesis that  $median(f(x) I_i^{(1)} - I_i^{(2)}) > 0$ , wherein said  $f(x)$  is a normalization factor;

computer program code for indicating whether said transcript is present based upon said  $p$ -value; and

15 a computer readable medium for storing said codes.

34. The computer program code of Claim 33 further comprising computer program code for calculating normalization factor, said code comprising:

code for obtaining the geometric mean ( $\bar{x}$ ) of said  $I_i^{(1)}$  and said  $I_i^{(2)}$ ;

20 code for calculating said normalization factor according to:

$f(x) = e^{h(x)}$ , wherein said  $h(x)$  is derived from referential intensities from said first and second probe arrays.

35. The computer software product of Claim 34 wherein said  $h(x)$  is derived by relating geometric means ( $x_i'$ ) of first referential intensities ( $RI_i^{(1)}$ ) in said first probe array and said second referential intensities ( $RI_i^{(2)}$ ) in said second probe array to:

$$y_i' = \log \left( \frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

36. The computer software product of Claim 35 wherein said code for relating comprising:  
computer code for sorting ( $x_i, y_i$ ) pairs according to  $x_i$  into a plurality ( $m$  number) of bins with no overlapping;  
computer code for computing medians ( $\bar{x}_k$ ) of  $x_i$ 's and medians ( $\bar{y}_k$ ) of  $y_i$ 's for each bin; and  
computer code for interpolating said medians ( $\bar{x}_k, \bar{y}_k$ ).

37. The computer software product of Claim 36 wherein said bins are of approximately equal size.

38. The computer software product of Claim 37 wherein said  $h(x)$  is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_i + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_i + 1], w = \frac{\bar{x}_{i+1} - x}{\bar{x}_{i+1} - \bar{x}_i} \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}, i = 1, \dots, m-1,$$

39. The computer software product of Claim 38 wherein said  $m$  is 3.